AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application.

1.-27. (Canceled)

28. (Original) A program for designing a physiologically active peptide capable of interacting with a target protein, allowing a computer to execute:

(a3) a step for exhaustively generating amino acid sequences of constant length, and randomly selecting amino acid sequences from among them for extraction as a library for analysis,

(b3) a step for calculating an intermolecular energy parameter for each of the amino acid sequences extracted as a library for analysis,

(c3) a step for generating a score matrix based on amino acid prevalence using an intermolecular energy parameter calculated in step (b3),

(d3) a step for calculating a score based on amino acid prevalence using a score matrix based on amino acid prevalence,

(e3) a step for conducting a correlation analysis between an intermolecular energy parameter calculated in step (b3) and said score to obtain a regression equation,

(f3) a step for converting a score matrix based on amino acid prevalence to a matrix based on an amino acid position-dependent intermolecular energy parameter using said regression equation,

(g3) a step for calculating an amino acid position-dependent intermolecular energy parameter value from a matrix based on an amino acid position-dependent intermolecular energy parameter, and

(h3) a step for extracting an amino acid sequence not higher than a specified amino acid position-dependent intermolecular energy parameter value.

29. (Currently Amended) ~~A~~ The program of claim 28, ~~for designing a physiologically active peptide capable of interacting with a target protein,~~ further allowing a computer to execute:

~~(a3') a step for exhaustively generating amino acid sequences of constant length, and randomly selecting amino acid sequences from among them for extraction as a library for analysis,~~

~~(b3') a step for calculating an intermolecular energy parameter for each of the amino acid sequences extracted as a library for analysis,~~

~~(c3') a step for generating a score matrix based on amino acid prevalence using an intermolecular energy parameter calculated in step (b3'),~~

~~(d3') a step for calculating a score based on amino acid prevalence using a score matrix based on amino acid prevalence,~~

~~(e3') a step for conducting a correlation analysis between an intermolecular energy parameter calculated in step (b3') and said score to obtain a regression equation,~~

~~(f3') a step for converting a score matrix based on amino acid prevalence to a matrix based on an amino acid position-dependent intermolecular energy parameter using said regression equation,~~

~~(g3') a step for calculating an amino acid position-dependent intermolecular energy parameter value from a matrix based on an amino acid position-dependent intermolecular energy parameter,~~

~~(h3') a step for extracting an amino acid sequence not higher than a specified amino acid position-dependent intermolecular energy parameter value,~~

~~(i3')~~ (i) a step for calculating an intermolecular energy parameter with a target site of target protein, for ~~an~~ the extracted amino acid sequence,

~~(j3')~~ (ii) a step for storing said amino acid sequence, along with said intermolecular energy parameter, ~~in a storage,~~

~~(k3')~~ (iii) a step for extracting a specified number of amino acid sequences on the basis of information stored by step (ii), ~~(j3'),~~ and

~~(l3')~~ (iv) a step for displaying an amino acid sequence extracted in step (iii) ~~(k3')~~ as a candidate for physiologically active peptide.

30. (Currently Amended) ~~A~~ The program of claim 29, further including between step (iii) ~~(k3')~~ and step (iv): ~~(l3'):~~

(I) a step for generating an amino acid sequence with an amino acid variation introduced to an amino acid sequence extracted in step (iii), ~~(k3'),~~

(II) a step for calculating an intermolecular energy parameter between an amino acid sequence generated in step (I) and a target site of target protein, and

(III) a step for comparing an intermolecular energy parameter calculated in step (II) with an intermolecular energy parameter between an amino acid sequence extracted in step (iii) ~~(k3')~~ and a target site of target protein as a control, and extracting an amino acid sequence having an intermolecular energy parameter that is more stable ~~stabler~~ than the intermolecular energy parameter of the control.

31. (Canceled)

32. (Currently Amended) An apparatus for designing a physiologically active peptide capable of interacting with a target protein, provided with (A3) a first amino acid sequence search portion, (B3) a first intermolecular energy calculation portion, (C3) a score matrix generation portion, (D3) a score calculation portion, (E3) a regression equation generation portion, (F3) a matrix conversion portion, (G3) an amino acid position-dependent energy calculation portion, (H3) a second amino acid sequence search portion, (I3) a second intermolecular energy calculation portion, (J3) an amino acid sequence memory portion, (K3) a third amino acid sequence search portion, and (L3) an amino acid sequence display portion, wherein:

said first amino acid sequence search portion includes (a3) ~~(a3')~~ a means of exhaustively generating amino acid sequences of constant length, and randomly selecting amino acid sequences from among them for extraction as a library for analysis,

said first intermolecular energy calculation portion includes (b3) ~~(b3')~~ a means of calculating an intermolecular energy parameter for each of the amino acid sequences extracted as a library for analysis,

said score matrix generation portion includes (c3) ~~(c3')~~ a means of generating a score matrix based on amino acid prevalence using an intermolecular energy parameter calculated by means (b3'),

said score calculation portion includes (d3) ~~(d3')~~ a means of calculating a score based on amino acid prevalence using a score matrix based on amino acid prevalence,

said regression equation generation portion includes (e3) ~~(e3')~~ a means of conducting a correlation analysis between an intermolecular energy parameter calculated by means (b3') and said score to obtain a regression equation,

said matrix conversion portion includes (f3) ~~(f3')~~ a means of converting a score matrix based on amino acid prevalence to a matrix based on an amino acid position-dependent intermolecular energy parameter using said regression equation,

said amino acid position-dependent energy calculation portion includes (g3) ~~(g3')~~ a means of calculating an amino acid position-dependent intermolecular energy parameter value from a matrix based on an amino acid position-dependent intermolecular energy parameter,

said second amino acid sequence search portion includes (h3) ~~(h3')~~ a means of extracting an amino acid sequence not higher than a specified amino acid position-dependent intermolecular energy parameter value,

said second intermolecular energy calculation portion includes (i) ~~(i3')~~ a means of calculating an intermolecular energy parameter with a target site of target protein, for an extracted amino acid sequence,

said amino acid sequence memory portion includes (ii) ~~(j3')~~ a means of storing said amino acid sequence, along with said intermolecular energy parameter, ~~in a storage,~~

said third amino acid sequence search portion includes (iii) ~~(k3')~~ a means of extracting a specified number of amino acid sequences on the basis of information stored by step (ii), ~~(j3'),~~ and

said amino acid sequence display portion includes (iv) ~~(l3')~~ a means of displaying an amino acid sequence extracted in step (iii) ~~(k3')~~ as a candidate for physiologically active peptide.

33. (Canceled)

34. (New) A method of designing a physiologically active peptide capable of interacting with a target protein, comprising:

(a3) a step for exhaustively generating amino acid sequences of constant length, and randomly selecting amino acid sequences from among them for extraction as a library for analysis,

(b3) a step for calculating an intermolecular energy parameter for each of the amino acid sequences extracted as a library for analysis,

(c3) a step for generating a score matrix based on amino acid prevalence using an intermolecular energy parameter calculated in step (b3),

(d3) a step for calculating a score based on amino acid prevalence using a score matrix based on amino acid prevalence,

(e3) a step for conducting a correlation analysis between an intermolecular energy parameter calculated in step (b3) and said score to obtain a regression equation,

(f3) a step for converting a score matrix based on amino acid prevalence to a matrix based on an amino acid position-dependent intermolecular energy parameter using said regression equation,

(g3) a step for calculating an amino acid position-dependent intermolecular energy parameter value from a matrix based on an amino acid position-dependent intermolecular energy parameter, and

(h3) a step for extracting an amino acid sequence not higher than a specified amino acid position-dependent intermolecular energy parameter value.

35. (New) The method of claim 34, which further comprises extracting, by method 1, complementary amino acid sequences for a target amino acid sequence of target protein and/or extracting, by method 2, an amino acid sequence of an optionally chosen length from the interaction region for the target protein, wherein the method 1 comprises:

(a1) a step for accepting an entry of sequence data on a target amino acid sequence,

(bl) a step for converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,

(cl) a step for generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those in step (bl),

(dl) a step for calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target: amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence,

(el) a step for storing a candidate for complementary amino acid sequence, along with said complementariness parameter, and

(fl) a step for extracting a specified number of complementary amino acid sequences on the basis of information stored by step (el), and the method 2 comprises:

(a2) a step for identifying the interaction region in a protein that interacts with a target site of target protein, and

(b2) a step for extracting an amino acid sequence of an optionally chosen length from said interaction region.

36. (New) The method of claim 35, wherein said complementariness parameter is the correlation coefficient between a moving average profile waveform for said target amino acid sequence and a complementary moving average profile waveform of a candidate for complementary amino acid sequence.

37. (New) The method of claim 35, wherein said amino acid index is one or more indices selected from among indices based on the degree of hydrophobicity, indices based on an electric property, indices showing the likelihood of taking the α-helix and β-sheet, and indices showing the relative size of side chain volume.

38. (New) The method of claim 35, characterized in that the number of candidates for complementary amino acid sequence extracted as physiologically active peptides is narrowed down by taking steps (bl) - (fl) for a specified number of complementary amino acid sequences extracted in steps (al) - (f1) using one or more specified amino acid indices, in one or more repeats, using one or more other amino acid indices.

39. (New) The method of claim 34, further comprising:

(i) a step for calculating an intermolecular energy parameter with a target site of target protein, for the extracted amino acid sequence,

(ii) a step for storing said amino acid sequence, along with said intermolecular energy parameter,

(iii) a step for extracting a specified number of complementary amino acid sequences on the basis of information stored by step (ii), and

(iv) a step for displaying an amino acid sequence extracted by step (iii) as a candidate for physiologically active peptide.

40. (New) The method of claim 39, further including between step (iii) and step (iv):

(I) a step for generating an amino acid sequence with an amino acid variation introduced to an amino acid sequence extracted in step (iii),

(II) a step for calculating an intermolecular energy parameter between an amino acid sequence generated in step (I) and a target site of target protein, and

(III) a step for comparing an intermolecular energy parameter calculated in step (II) with an intermolecular energy parameter between an amino acid sequence extracted in step (iii) and a target site of target protein as a control, and extracting an amino acid sequence having an intermolecular energy parameter that is more stable than the intermolecular energy parameter of the control.

41. (New) The program of claim 28, further allowing a computer to execute following steps (al) - (fl):

(al) a step for accepting an entry of sequence data on a target amino acid sequence of target protein,

(bl) a step for converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,

(cl) a step for generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those in step (bl),

(dl) a step for calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence,

(el) a step for storing a candidate for complementary amino acid sequence, along with said complementariness parameter, and

(fl) a step for extracting a specified number of complementary amino acid sequences on the basis of information stored by step (el), and/or following steps (a2) - (b2):

(a2) a step for identifying the interaction region in a protein that interacts with a target site of target protein, and

(b2) a step for extracting an amino acid sequence of an optionally chosen length from said interaction region.

42. (New) The program of claim 41, wherein said complementariness parameter is the correlation coefficient between a moving average profile waveform for said target amino acid sequence and a complementary moving average profile waveform of a candidate for complementary amino acid sequence.

43. (New) The program of claim 41, wherein said amino acid index is one or more indices selected from among indices based on the degree of hydrophobicity, indices based on an electric property, indices showing the likelihood of taking the α-helix and β-sheet, and indices showing the relative size of side chain volume.

44. (New) The program of claim 41, characterized in that the number of candidates for complementary amino acid sequence extracted as physiologically active peptides is narrowed down by taking steps (bl) - (fl) for a specified number of complementary amino acid sequences extracted in steps (al) - (fl) using one or more specified amino acid indices, in one or more repeats, using one or more other amino acid indices.

45. (New) A computer-readable recording medium containing the program of claim 28.

46. (New) The apparatus of claim 32, for processing the amino acid sequences extracted by step (f1) and/or (b2) in the second intermolecular energy calculation portion, the amino acid sequence memory portion, the third amino acid sequence search portion, and the amino acid sequence display portion, further provided with following constitution 1:

(A) a data entry portion, (B) a data editing portion, (C) a complementary amino acid sequence candidate generation portion, (D) a complementariness calculation portion,. (E) a complementary amino acid sequence candidate memory portion, and (F) a complementary amino acid sequence search portion, and/or following constitution 2:

(A2) an interaction region identification portion, and (B2) a first interaction region amino acid sequence search portion, wherein, in said constitution 1:

said data entry portion includes (al) a means of accepting an entry of sequence data on a target amino acid sequence,

said data editing portion includes (bl) a means of converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,

said complementary amino acid sequence candidate generation portion includes (cl) a means of generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those for means (bl),

said complementariness calculation portion includes (dl) a means of calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence,

said complementary amino acid sequence candidate memory portion includes (el) a means of storing a candidate for complementary amino acid sequence, along with said complementariness parameter,

said complementary amino acid sequence search portion includes (fl) a means of extracting a specified number of complementary amino acid sequences on the basis of information stored by means (el),

said interaction region identification portion in said constitution 2 includes (a2) a means of identifying the interaction region in a protein molecule that interacts with a target site of target protein,

said first amino acid sequence search portion includes (b2) a means of extracting an amino acid sequence of an optionally chosen length from said interaction region.